REMARKS

Applicants have canceled Claims 92 and 99-111 without prejudice or disclaimer; withdrawn Claims 112-123 without prejudice or disclaimer; and have amended Claims 87 and 93. Enabling support for the amended claims can be found in the application as filed, and therefore no new matter is contained in the amendments. Reconsideration of the present application and allowance of resulting Claims 87-91, and 93-98 is respectfully requested in view of the amendments and following remarks.

I. Claim Rejections under 35 U.S.C. § 112, first paragraph, enablement requirement

The Office Action has rejected Claims 87-111 under 35 U.S.C. §112, first paragraph as failing to comply with the enablement requirement.

Claims 92 and 99-111 have been cancelled without prejudice or disclaimer, and therefore the rejection is moot with respect to those claims. Applicants reserve the right to prosecute the subject matter in these claims in one or more continuation or divisional applications.

The Office Action states "the specification fails to provide an enabling disclosure for the claimed compositions and methods of making said compositions because methods of transplantation of neural tissue or other cells into the CNS or PNS are not routinely successful and the specification does not offer adequate guidance to enable one skilled in the art to practice the claimed invention to derive a therapeutic benefit in a disease animal. The specification teaches that the only use for the claimed compositions is for transplantation to produce a therapeutic effect but the specification does not adequately teach how to use the claimed method to produce such an effect. . . . While the specification discloses the use of human cord blood

fractions that have been used either directly upon thawing (cord blood mononuclear cells) or treated in culture for a week with various trophic factors (BDNF, NGF, EGF+bFGF) prior to transplantation into a rat stroke model (pages 58-65), the claims cover the preparation of a great variety of cell compositions, including terminally-differentiated cells, which the specification does not teach how to use. . . . The specification fails to provide specific guidance for using the great variety of cell compositions covered by the claims, to provide a therapeutic benefit for the treatment of a disease or disorder."

Applicants respectfully traverse the rejection as follows. The Office Action asserts that the specification does not teach how to use the claimed compositions therapeutically for the treatment of any disorder. However, the current claims are directed to methods of generating differentiated cells from human umbilical cord blood, and are not directed to methods of therapy. Applicants are not required to isolate and test the therapeutic benefit of every neural cell that can be derived from HUCB cells. Applicants have developed methods for deriving neural cells from HUCB cells that are at least useful for generating and isolating proteins produced at various stages of neural cell differentiation, and for permitting recombinant production of polypeptides. The generation and isolation of proteins associated with particular stages of neural differentiation and the recombinant production of polypeptides are routine for one of ordinary skill in the art. As such, the cells generated using the claims of the current invention are enabled for use in at least therapeutic research.

The Office Action also states "With regard to the cells that were cultured with various trophic factors, the specification does not disclose the phenotype of these cells and the claims require the production of cells that exhibit an increase in the expression of genes associated with neurogenesis." Applicants respectfully traverse this statement as follows.

The current specification teaches the culture of human cord blood with a number of differentiation agents in order to produce neural cells, and compositions comprising the neural cells derived from human cord blood cells. For example, the specification teaches the isolation of human cord blood cells, which were thawed and plated in minimal essential medium (page 37). After 24-72 hours, the medium was replaced with serum free "Neural Proliferation Medium," consisting of N2 medium supplemented with glucose, insulin, transferrin, progesterone, putrescine, selenium chloride, glutamine, sodium bicarbonate, HEPES, heparin, EGF and bFGF. The cultures were then exposed to "Neural Differentiation Medium," which was the Neural Proliferation Medium without EGF and bFGF, but instead containing retinoic acid (RA) plus NGF. RNA was isolated from the cells treated with or without the RA+NGF, and the cells were also examined with antibodies to neural markers. Cells treated with RA+NGF showed higher levels of RNA and protein for a number of neural markers than was observed in control cells treated with DMEM. For example, using a gene chip, a total of 322 genes were up-regulated or down-regulated by at least a factor of 2 (pg. 40, lines 5-7). The greatest degrees of up-regulation were noted for pleiotrophin, glypican-4, neuronal pentraxin II, neuronal growth associated protein 43, and neuronal PAS1 (page 40, lines 6-15). By immunohistochemistry, it was shown that a significant proportion of cells in the RA+NGF treated cultures were positive for Musashi-1, β-tubulin III, GFAP, while the DMEM treated cells were not immunoreactive for these markers. Densitometric analysis of Western blots showed that NGF+RA treatment increased protein expression of Musashi-1, β-tubulin III, pleiotrophin and NeuN (page 40, lines 10-25). This example demonstrates that neural cells are readily derived from human cord blood cells using differentiation agents. The cells express a number of neural markers, including nestin, a marker for neuronal precursors, GFAP, a marker for astrocytes, and NeuN, a neuron specific marker. As such, Applicants have demonstrated that culturing human cord blood cells

with trophic factors results in the production of cells that exhibit an increase in the expression of genes associated with neurogenesis that can readily be used for transplantation and for other therapeutic research purposes.

For at least the foregoing reasons, and considering the amendments to the claims, Applicants respectfully request reconsideration and removal of the rejection and allowance of Claims 87-91 and 93-98.

II. Claim Rejections under 35 U.S.C. § 112, second paragraph, definiteness requirement

The Office Action has rejected Claims 87-111 under 35 U.S.C. §112, second paragraph, as failing to comply with the definiteness requirement.

The Office Action rejected Claims 87-111 as indefinite for the recitation of "increase" and "decrease," asserting that "it is unclear what would be considered the reference state for said "increase" or said "decrease"." Claims 92 and 99-111 have been cancelled without prejudice or disclaimer, and therefore the rejection is moot with respect to these claims. Applicants have amended Claim 87 and dependent claims to provide a reference state for "increase" and "decrease" and submit that the amendments overcome the rejections.

III. Claim Rejections under 35 U.S.C. § 102

The Office Action rejected Claims 99-111 under 35 U.S.C. §102(a) as being anticipated by Kopen et al. (1999).

Claims 99-111 have been canceled and therefore the rejection is moot with respect to those claims. Applicants reserve the right to prosecute the subject matter in these

claims in one or more continuation or divisional applications.

The Office Action rejected Claims 99-111 under 35 U.S.C. §102(b) as being anticipated by Reynolds et al. (1992).

Claims 99-111 have been canceled and therefore the rejection is moot with respect to those claims. Applicants reserve the right to prosecute the subject matter in these claims in one or more continuation or divisional applications.

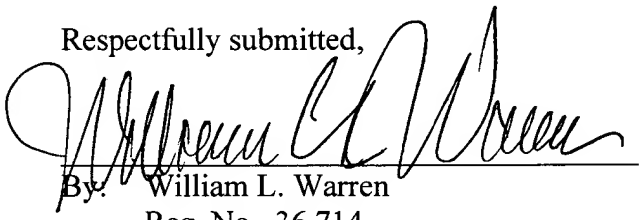
The Office Action rejected Claims 99-111 under 35 U.S.C. §102(b) as being anticipated by Azizi et al. (1998).

Claims 99-111 have been canceled and therefore the rejection is moot with respect to those claims. Applicants reserve the right to prosecute the subject matter in these claims in one or more continuation or divisional applications.

For at least the foregoing reasons, Applicants respectfully request reconsideration and removal of the rejections and allowance of Claims 87-91 and 93-98. The foregoing is submitted as a full and complete Response to the Final Office Action mailed September 23, 2004. No additional fees are believed due; however, the Commissioner is hereby authorized to charge any additional fees that may be required, or credit any overpayment to Deposit Account No. 19-5029.

This Response places all claims in the present application in condition for allowance, and such action is courteously solicited. The Examiner is invited and encouraged to contact the undersigned attorney of record if such contact will facilitate an efficient examination and allowance of the application.

Respectfully submitted,



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